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Office of Toxic Substances (TS-790)
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401 M Street, S.W.
Washington, DC 20460

Attn: Section 8(e) Notification Coordinator

Re: Substantial Risk Report on 4,4'-Methylenediphenyl-Diisocyanate (MDI)
CAS Number: 101-68-8

This letter and attachment summarize information from ICI Americas Inc. (ICIA) subject to reporting under Section 8(e) of the Toxic Substances Control Act (TSCA). Attached is an abstract submitted for presentation at a meeting of the British Occupational Hygiene Society. This abstract reports some results from a study conducted at the Fraunhofer Institute of Toxicology and Aerosol Research, Hannover Germany. This study is not sponsored by ICIA or our parent company ICI, PLC. The authors report findings from lung lavage and pulmonary function measurements following exposure of rats by inhalation (18 hrs/day, 5 days/wk, for 90 days) to 1, 3 mg/M^3 of MDI aerosol.

This abstract is the only information we have available on this study. We are, however, sharing this information with other producers of MDI.

We have reviewed our product literature and believe the present TLV for MDI (0.05 mg/M^3) offers sufficient protection against long term and short term affects. Our MSDS for MDI currently reflects known health hazards including respiratory sensitization and the potential for permanent decreases in lung function.

Questions related to this submission may be directed to Joseph F. Jadlocki, ICIA Product Safety Supervisor at (302)886-5184.

Respectfully submitted,

Samuel E. Malovrh
Director, Environmental Affairs

JFJ/kt/as7
Attachments

THE BRITISH OCCUPATIONAL HYGIENE SOCIETY

PAPER NUMBER - P 6.8

INHALATION EXPOSURE OF RATS TO 4,4'-METHYLENEDIPHENYL-DIISOCYANATE (MDI)

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To guide in determination of the concentration levels to be employed in a chronic inhalation study a 90-day study using three different exposure concentrations of MDI (0.3, 1.0, 3.0 mg/m³) was performed. Equipment for the generation of monomeric MDI has been developed. The MDI-aerosol was generated by using an evaporation-condensation technique consisting of the following steps. Firstly, the monomeric MDI which is a solid at room temperature is liquidized at 50 °C and nebulized resulting in relatively large droplets. Subsequently the droplets are evaporated leaving behind the corresponding number of small residue particles originating from nonvolatile impurities in the test substance. The vapor is then forced to recondens onto these nuclei by turbulent mixing with cool dilution air. The kinetics of condensation lead to considerably finer aerosol. Polymerization of the test material is prevented because MDI is exposed to elevated temperatures only for the short time of droplet evapoartion (1.5 sec). The "primary" aerosol is then router into a buffer chamber where 3 ejection nozzles perform a first dilution corresponding to the three desired dose levels. The final dilutuion of the test is performed immediately prior to entering the inhalation chambers. This generation technique delivers a stable quasi-monodisperse aerosol with a MMAD of 1.1 µm and a geometric standard deviation of 1.37. The particle size distribution is measured using a 9-stage "Berner" low pressure impactor. The total mass concentration in each inhalation chamber was monitored using light scattering aerosol sensors, which were calibrated by means of gravimetric analysis of filter samples.
For analytical chemistry MDI aerosol was collected on PTFE filters and extracted by acetonitrile; gaseous MDI which according to the vapor pressure of MDI occurs in a concentration of approx. 100 µg/m³ is collected by drawing the air sample through a glass tube filled with glas wool which is imprignated with the derivatization agent, 4-nitro-N-propylbenzylamin (NPBA). The determination of MDI is carried out by high performance liquid chromatography (HPLC) and UV-detection after derivatization with NPBA at room temperature. Using reversed phase column and acetonitrile (A) and water (B) as eluents the derivatized compound is detected at 275 nm. The detection limit is 1 ng.
After exposing the female Wistar rats 18 hrs/day and 5 days per week for 90 days the following effects were observed: slightly lower body weight gain; increase of the wet and dry lung weight after 1 and 3 mg/m³ exposure; total cell count of bronchio-alveolar lavage (BAL) as well as the percentage of granulocytes and lymphocytes from highest dose group was clearly higher and the percentage of macrophages was reduced. Total protein, β-glucoronidase and lactate dehydrogenase in BAL was also elevated in the high dose group. Mechanical lung function measurements using the whole body plethysmograph and the anesthetized, spontaneously breathing rat showed a larger funtional residual capacity and residual volume, decreased quasistatic lung compliance and CO diffusing capacity after 3 mg/m³ exposure. The histopathological investigation revealed submucosal infiltration of mononuclear cells, goblet-cell hyperplasia and erosion of the respiratory epithelium in nasal and paranasal sinai and hyperplasia of the bronchus associated lymphatic tissue and inflammatory alterations in the lungs. These effects occurred after exposure to 1 and 3 mg/m³.

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